

# Antidepressant Controlled Trial for Negative Symptoms in schizophrenia

<b>Submission date</b> 12/05/2010	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 12/05/2010	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
<b>Last Edited</b> 03/06/2016	<b>Condition category</b> Mental and Behavioural Disorders	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Schizophrenia is a mental health problem usually starting in the late teens or early twenties, and often lasting many years. It affects behaviour, thinking and perception, and in more severe cases it affects a person's ability to socialise, work and carry out routine daily tasks appropriately. The best known features of schizophrenia are 'positive' symptoms such as false beliefs ('delusions') and hallucinations (most commonly, hearing voices). But also common are the so-called 'negative' symptoms, which appear to reflect a loss of a person's usual emotional expressiveness and responsiveness, spontaneity of speech, and drive. These can affect a person's ability to relate to other people and get on with day-to-day tasks. The standard medication ('antipsychotics') is usually helpful for this illness, and if taken continually over time can keep people well, reducing the likelihood of further episodes. However, the positive symptoms tend to be more likely to improve with this medication than the negative symptoms, and so a proportion of people with schizophrenia, perhaps around 1 in 5, will have continuing negative symptoms. If antipsychotic medication alone does not help negative symptoms for a particular person, there are no other established medications that we know can help. However, there is some evidence that antidepressant medication, usually given to treat depression, might also reduce negative symptoms if added to antipsychotic medication, and not produce too many problems with side effects. What is not clear is whether any improvement in negative symptoms is also accompanied by an improvement in a person's quality of life, and how long it might take for that to be evident. The evidence mainly comes from research studies where an antidepressant was added to antipsychotic medication over a relatively short period, and no longer than three months. These studies have reported any changes observed in negative symptoms but not whether there was any effect on a person's quality of life. Also, not all of these studies have carefully distinguished whether any improvement seen is specific to negative symptoms or due to change in other symptoms of schizophrenia or side effects of antipsychotic medication, which can all look very similar. We plan to carry out a study which will try to overcome these limitations of previous studies.

### Who can participate?

Patients aged 18 – 75 with schizophrenia who are being treated with antipsychotic medication but are experiencing continuing negative symptoms

What does the study involve?

Participants are randomly allocated to have either an antidepressant (citalopram) or a dummy tablet (placebo) added to the antipsychotic medication that they are already receiving, for a year. We have chosen citalopram as the antidepressant because while there is no reason to think that one antidepressant is likely to work better than another, citalopram is one of the least likely to cause problems by interacting with antipsychotic medication. By carefully assessing all the relevant symptoms and side effects regularly over the year of treatment and comparing those people taking the antidepressant with those given the placebo, we should be able to see if the antidepressant has had any effect on quality of life or negative symptoms. Also, we should gain a greater understanding of any positive effects of adding an antidepressant to antipsychotic treatment on a person's ability to live and work in the community, as well as the possible risks with regard to side effects.

What are the possible benefits and risks of participating?

Not provided at time of registration

Where is the study run from?

Imperial College London (UK)

When is the study starting and how long is it expected to run for?

June 2010 to December 2011

Who is funding the study?

Health Technology Assessment Programme (UK)

Who is the main contact?

Prof. Thomas Barnes

## Contact information

**Type(s)**

Scientific

**Contact name**

Prof Thomas Barnes

**Contact details**

Department of Psychological Medicine

The Reynolds Building

St. Dunstons Road

London

United Kingdom

W6 8RP

## Additional identifiers

**EudraCT/CTIS number**

2009-009235-30

**IRAS number**

**ClinicalTrials.gov number**

NCT01032083

**Secondary identifying numbers**

HTA 07/83/01; 7155

## **Study information**

**Scientific Title**

A multicentre randomised interventional trial of the clinical and cost-effectiveness of citalopram versus placebo in the management of negative symptoms of schizophrenia

**Acronym**

ACTIONS

**Study objectives**

The ACTIONS study is a multi-centre, double-blind, placebo-controlled, randomised clinical trial. The main aim of the study is to establish the clinical and cost-effectiveness of the selective serotonin reuptake inhibitor (SSRI) antidepressant, citalopram, in the management of negative symptoms of schizophrenia. The research hypothesis to be tested is that augmentation of stable antipsychotic medication with citalopram, is clinically and cost-effective for ameliorating persistent negative symptoms in schizophrenia and is not associated with an additional side effect burden.

More details can be found at: <http://www.nets.nihr.ac.uk/projects/hta/078301>

Protocol can be found at: [http://www.nets.nihr.ac.uk/\\_\\_data/assets/pdf\\_file/0018/51930/PRO-07-83-01.pdf](http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0018/51930/PRO-07-83-01.pdf)

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Charing Cross Research Ethics Committee, 21/08/2009, ref: 09/H0711/81

**Study design**

Multicentre randomised interventional treatment trial

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet

## **Health condition(s) or problem(s) studied**

Topic: Mental Health Research Network; Subtopic: Schizophrenia; Disease: Schizophrenia

## **Interventions**

Participants will be randomly assigned to receive additional treatment with either citalopram or identical placebo. Treatment with citalopram will be initiated at 20 mg/day for the first 4 weeks (or one placebo capsule), followed by the option to increase the dose to 40 mg per day (or two placebo capsules) for the remainder of the study period, i.e. daily for up to a year. If there are problems with tolerability, the clinician can reduce the dose back to 20 mg/day (or one placebo capsule).

Follow-up length: 12 months

Study entry: single randomisation only

## **Intervention Type**

Drug

## **Phase**

Not Applicable

## **Drug/device/biological/vaccine name(s)**

Citalopram

## **Primary outcome measure**

PANSS, measured at 3 months and 12 months

## **Secondary outcome measures**

1. Mental state
2. Social function
3. Service engagement
4. Medication

All outcomes scales relevant to the secondary outcomes will be administered at baseline and subsequently at 3, 9 and 12 months.

## **Overall study start date**

01/06/2010

## **Completion date**

01/12/2011

# **Eligibility**

## **Key inclusion criteria**

1. An Operational Criteria Checklist for Psychosis (OPCRIT) diagnosis of schizophrenia, schizophreniform, schizoaffective disorder or psychosis not otherwise specified (NOS) as defined by Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)

2. A negative subscale score of 20 or more on the Positive and Negative Syndrome Scale for Schizophrenia (PANSS). At least three of the seven items on the negative symptom subscale should be rated 3 or more. Negative symptoms that reflect, sometimes very subtly, manifestations of depressive symptoms, antipsychotic side effects such as bradykinesia, or positive symptoms, are referred to as secondary negative symptoms, and the assessors will attempt to distinguish these from primary negative symptoms. However, persistent negative symptoms will be used as an inclusion criterion rather than primary negative symptoms, as the former are the clinically-relevant target, and the latter represent a hypothesis about aetiology that cannot be definitely determined on cross-sectional assessment.
3. Aged 18 - 75 years, inclusive, either sex
4. Clinically stable for the last 3 months with a consistent antipsychotic regimen
5. Competent and willing to provide written, informed consent

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Planned sample size: 360; UK sample size: 360

**Key exclusion criteria**

1. Any medical contraindications to an SSRI antidepressant
2. Currently receiving antidepressant or clinician wants to treat with an antidepressant
3. Currently fulfil criteria for major depressive disorder; alcohol/substance hazardous use or dependence in past 3 months
4. Treated with ECT in the last 8 weeks
5. Cognitive or language difficulties that would preclude subjects providing informed consent or compromise participation in study procedures

**Date of first enrolment**

01/06/2010

**Date of final enrolment**

01/12/2011

**Locations****Countries of recruitment**

England

United Kingdom

**Study participating centre**  
**Imperial College London**  
London  
United Kingdom  
W6 8RP

## **Sponsor information**

**Organisation**  
Imperial College London (UK)

**Sponsor details**  
ICCH Building  
59 North Wharf Road  
London  
England  
United Kingdom  
W2 1LA

**Sponsor type**  
University/education

**Website**  
<http://www3.imperial.ac.uk/>

**ROR**  
<https://ror.org/041kmwe10>

## **Funder(s)**

**Funder type**  
Government

**Funder Name**  
Health Technology Assessment Programme

**Alternative Name(s)**  
NIHR Health Technology Assessment Programme, HTA

**Funding Body Type**  
Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

## Results and Publications

**Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date**

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**

Not provided at time of registration

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/04/2016		Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No